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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,040	11/15/2000	Paul J. Carter	11669.185USD3	5212

7590 08/07/2006

Katherine M. Kowalchyk  
P.O. Box 2903  
Minneapolis, MN 55402-0903

EXAMINER
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BLANCHARD, DAVID J

ART UNIT	PAPER NUMBER
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1643

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/714,040

Applicant(s)

CARTER, PAUL J.

Examiner

David J. Blanchard

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 25, 39-44 and 49-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 40-42 is/are allowed.
- 6) ☒ Claim(s) 25, 39, 43-44 and 49-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Prosecution on the merits of this application is reopened. Claims 25, 39, 43-44 and 49-52 are considered unpatentable for the reasons indicated below.
2. Claims 1-24, 26-38 and 45-48 are cancelled.  
  
Claims 25 and 44 are presently amended.  
  
Claims 49-52 have been added.
3. Claims 25, 39-44 and 49-52 are pending and under examination.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. This Office Action contains New Grounds of Rejections.

### ***Withdrawn Objections/Rejections***

6. The rejection of claims 25, 38, 44 and 46-48 under 35 U.S.C. 102(b) as being anticipated by Bodmer et al (WO 89/01974, 3/9/1989) is withdrawn in view of applicants arguments and amendments to the claims.
7. The rejections of Claims 25, 29 and 38-39 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "wherein the amino acid sequence of about 1 to 10 amino acids comprises a C terminal amino acid sequence Cys-X-X, wherein X is Ala, Arg, Pro or Asp" is withdrawn in view of the amendments to the claims.

8. The rejections of Claims 25, 29 and 38-39 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "A composition produced by the process" is withdrawn in view of the amendments to the claims.

9. The rejection of claim 47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter is withdrawn in view of the cancellation of the claim.

***New Grounds of Rejections***

10. The specification at pg. 29, lines 32-33 is objected to as disclosing the sequence Cysteine followed by two prolines and another Cysteine as being represented by "CPC" and not CPPC.

Appropriate correction is required.

11. Claims 25, 39, 43-44 and 49-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing NEW MATTER. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a composition comprising a monospecific F(ab')<sub>2</sub> that comprises a first and second Fab' each comprising a CH1 domain fused to an amino acid sequence of up to 10 amino acids that comprises a C-terminal amino acid

sequence of Cys-Ala-Ala. There is insufficient written support for the limitation of a CH1 fused to an amino acid sequence of up to 10 amino acids that comprise a C-terminal sequence of Cys-Ala-Ala. The as filed specification discloses at pg. 11 that the Cys-X-X sequence where X is preferably Ala is fused to the C-terminus of the CH1 of Fab'.

Further, at pg. 20, lines 4-7, the specification discloses that the heavy chain constant domain downstream from CH1 is deleted and the CH1 domain is followed C-terminally by Cys-Ala-Ala. The only disclosure of 10 amino acid residues is found at pg. 11, lines 25-27, where it is disclosed that the hinge may be entirely omitted in favor of one or more cysteine residues or, preferably short (about 1-10 residues) cysteine-containing polypeptide. Thus, the specification as filed only provides adequate written support for a F(ab')<sub>2</sub> comprising a first and second Fab' each comprising a CH1 domain fused directly to the amino acid sequence Cys-Ala-Ala. Additionally, the as filed specification discloses at pp. 29-30 that in order to express the Fab' fragment of huMab4D5-8 the CH1 gene segment was extended to encode part of the cysteine-containing antibody hinge region where cysteine followed by two prolines and another cysteine was chosen (interpreted as CPPC). To prevent the formation of an intramolecular disulfide bond between the two cysteine residues of the CPPC sequence construction of a Fab' variant with a single hinge cysteine residue having the C-terminal sequence Cys-Ala-Ala was produced (see pg. 30, lines 23-27). Thus, while the Fab' variant comprising the CH1-Cys-Ala-Ala sequence, which is three amino acids in length and within the genus of a CH1 domain fused to up to 10 amino acids comprising the C-terminal sequence Cys-Ala-Ala, this does not provide adequate written support for the broader genus of

sequences that are up to 10 or about up to 10 amino acids comprising the C-terminal sequence Cys-Ala-Ala as presently claimed because there is insufficient written description for the sequences contained therein. A subgenus is not necessarily described by a genus encompassing it and a species upon which it reads. *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972). Instant claims 25, 39, 43-44 and 49-52 recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in claims 25, 39, 43-44 and 49-52, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claims 25, 39, 43-44 and 49-52 in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

### ***Conclusion***

12. The following art made of record and not relied upon is considered pertinent to applicant's disclosure.

Carter P. et al. Bio/Technology, 10(2) :163-167, February 1992.

13. Claims 40-42 are free of the prior art.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00

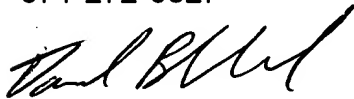
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AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,  
David J. Blanchard  
571-272-0827



SHEELA HUFF  
PRIMARY EXAMINER